REMARKS

The Final Office Action mailed March 4, 2004, has been received and reviewed. Claims 1 through 15 are currently pending in the application. Claims 1 through 15 stand rejected. Responsive thereto, the proposed amendments were made in respect to the original patent and in compliance with 37 CFR 1.173. The proposed amendments are indicated above with the following changes over the previous version:

Specifically, in claim 1, line 1 the phrase "consisting of" was added over the previous version. In claim 1, lines 4-6, the phrase "wherein said contiguous LHRH decapeptide sequences are joined with a terminus to terminus linkage" was added over the previous version. Support for the amendments is found in Column 9 of the specification where, under Experiment 1, the specification describes the testing of LHRH dimers and multimers. Experiment 1 included an N-tandem LHRH dimer (Column 9, line 26), and a C-tandem LHRH dimer (Column 9, line 17). As such, the specification would allow one skilled in the art to conclude the inventor had possession of the amended claim 1.

In claim 2, line 1 the phrase "according to claim 1" was removed, and at lines 8 and 9 the phrase "wherein said contiguous LHRH decapeptide sequences are joined with a terminus to terminus linkage" was added. Similar to support for changes to claim 1, support for these claim 2 amendments is found in Column 9 of the specification where, under Experiment 1, the specification describes the testing of LHRH dimers and multimers.

In claim 3, the phrase "[p]eptides according to claim 1" was removed making this an independent claim. The phrase "A peptide that comprises at least two contiguous LHRH decapeptide sequences wherein the amino acid glycine at position 6 of at least one of the constituting LHRH decapeptides is replaced by a dextrorotatory amino acid with a side chain that can be coupled to a carrier compound wherein said decapeptides are joined with an N-terminus to N-terminus linkage, or C-terminus to C-terminus linkage and" was added over the previous version. Support for this amendment is found in Experiment 1, columns 9 and10, of the original patent specification. Experiment 1 tested tandem LHRH sequences with D-Lys replacing at least one of the glycine at position 6. As such, the specification would allow one skilled in the art to conclude the inventor had possession of the amended claim 3.

In claim 4, "(SEQ ID NO: 4)" was added to the claim to correct an unintentional omission error.

In claim 5, line 1, the phrase "according to claim 3 and" was removed from the previous version. In line 8, the phrase "the pyroglutamic acid residue at position 1 of LHRH is replaced with a glutamine and a cysteine is placed before the glutamine at position 1 in LHRH and" was added over the previous version. Support for the amendment to claim 5 is found in the specification under Experiment 1 at column 9, number 3. Here the specification discloses an LHRH where the pyroglutamic acid residue at position 1 of LHRH was replaced with a glutamine, and a cysteine was placed in front of the glutamine at position 1. Thus allowing one skilled in the art to conclude the inventor had possession of the amended claim 5.

In claim 9, line 1, the word "composition" was removed, and the word "peptide" was added. This amendment is supported in the original patent specification in column 3, line 62-67, where the LHRH peptide is describe in sufficient detail to allow one of skill in the art to believe that the inventor has possession of the LHRH peptide.

In claim 9, line 1, the word "claims" was removed and replaced with "claim" to correct an unintentional error, because the word "claim" refers to only a singular "claim 1" and not multiple claims.

In claim 9, line 2, the phrase "additionally comprising" was removed and replaced with the word "combined" to more distinctly point out and claim the subject matter. This amendment is supported in the disclosure at column 6, lines 45-47, where the LHRH peptide is described as also being combined with an immunoadjuvant.

In claims 10 and 11, the word "composition" was removed, and the word "peptide" was added. These amendments are supported in the original patent specification in column 3, line 62-67, where the LHRH peptide is describe in sufficient detail to allow one of skill in the art to believe that the inventor has possession of the peptide.

In claim 14, the word "effect" was removed and replaced with the word "affect." This amendment was made to correct an unintentional spelling error.

Finally, applicants assert that this amendment introduces no new matter and respectfully request reconsideration of the reissue application.

37 C.F.R 1.175(b)(1) Reissue Oath/Declaration is defective

Claims 1-15 are rejected as based upon a defective reissue declaration under 37 C.F.R. 1.175(b)(1). Upon receipt of the signed Reissue Declaration, applicants will immediately submit a complete supplemental Reissue Oath/Declaration pursuant to 37 C.F.R. 1.175(b)(1). Applicants respectfully thank the Examiner for his patience in this matter.

Specification

The telephone conversation with the Examiner on May 3, 2004, in regards to the claim for priority objection, was much appreciated. Applicants amended the first paragraph of column 1 to reflect the discussed recommendations, and respectfully request this objection be removed. Specifically, the amended first paragraph correctly claims priority under 35 U.S.C. § 120 from PCT International Application Number PCT/NL96/00223 filed on June 6, 1996, designating the United States of America which itself is a continuation in part from both U.S. Patent Application Serial No. 08/477,298 filed on June 7, 1995, now abandoned, and U.S. Patent Application Serial No. 08/476,013, filed on June 7, 1995, now abandoned

Furthermore, applicants have amended the specification in accordance with the Examiner's suggestions to correct typographical and clerical errors. Applicants respectfully request reconsideration of the specification.

35 U.S.C. 112 second paragraph

Claims 5, 9, and 10 are rejected under 35 U.S.C. 112, second paragraph. Applicants respectfully traverse this rejection.

Applicants have amended claims 5, 9, and 10 to make them definite and to particularly point out and distinctly claim the subject matter. Specifically, instant amended claim 5 is no longer dependent from claim 3, removing the alleged indefiniteness of the peptide in claim 5 with respect to naturally occurring LHRH. Furthermore, at claim 5, line 7, the "D-glycine" was replaced with "D-lysine" to correct an unintentional transcription error.

In Claim 9, the phrase "additionally comprising" was replaced with "combined" to remove the alleged indefiniteness about how a peptide can comprise a mild adjuvant.

Finally, in claim 10, the indefiniteness was removed by replacing "composition" with "peptide" so as to correctly refer to the peptide of claim 9.

As such, the proposed amendments should remove the alleged indefiniteness and applicants respectfully request that the rejection of claims 5, 9, and 10 be withdrawn.

Claim Objections

Applicants, per the Examiner's request, have corrected the informalities regarding the text of claims 2-5. Specifically, SEQ ID NOS were originally inserted into the claims by preliminary amendments but were unintentionally omitted from the listing of claims filed on January 16, 2004. Also, in claim 2, line 1, the word "and" was changed back to "an." At claim 3, line 5 the word "an" was changed back to "a." Furthermore, the upper residue numbers in claims 4 and 5 were correctly aligned. And finally, at claim 5, line 7; "D-glycine" was changed back to the appropriate "D-lysine." Applicants respectfully requests that objections to claims 2-5 be removed.

Improper dependant form under 37 CFR 1.75(c)

Applicants have amended claim 5, as suggested by the Examiner in paragraph 11 of the Communication, to be an independent claim by removing the dependent reference to claim 3. Applicants respectfully request that this objection to claim 5 be removed.

35 U.S.C. § 103(a) Obviousness Rejection

Obviousness Rejection Based on U.S. Patent 5,723,129 to Potter *et al.* in view of the GB patent 2,228,262 or the GB Patent 2,196,969.

Claims 1 and 6-15 are rejected under 35 U.S.C. 103(a) as being obvious over Potter *et al.* (U.S. Patent 5,723,129) in view of the GB Patent 2,228,262 or the GB Patent 2,196,969. Applicants respectfully traverse this rejection.

Claims 6-15 ultimately depend on independent claim 1. If independent claim 1 can be shown to be nonobvious then those claims dependent from claim 1 will also be nonobvious.

M.P.E.P. 706.02(j) sets forth the standard for a section 103(a) rejection:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be in the prior art, and not based on applicant's disclosure. *In re Vaeck,* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

The 35 U.S.C. § 103(a) obviousness rejections of claims 1 and 6-15 are improper because the references relied upon by the Examiner fail to suggest or motivate the combination of the references.

The suggested combination of the '262 and '269 Patents, teach a dimer of the [D-amino acid^6]GnRH linked by the centrally located D-amino acid^6 side chains. Potter *et al.* teaches terminus to terminus linked GnRH multimers fused to a leukotoxin. The GB Patents teach that their GnRH dimer conjugate with the unique linkage site at a centrally located amino acid, make it more immunogenic than other embodiments (see GB Patent '262, page 5, lines 17-25). As such, the GB patents teach away from a terminus to terminus linkage as disclosed in Potter *et al.*, and are a motivation not to combine the suggested references. Therefore, there is no suggestion or motivation to combine the references Potter *et al.*, in light of G.B. Patents '262 and '269.

Moreover, the obviousness rejection of claims 1 and 6-15 is improper because Potter *et al.*, in light of G.B. Patents '262 and '269, fail to teach or suggest all the elements of the instant amended claim 1. Potter *et al.* discloses chimeric proteins comprising a leukotoxin fused to GnRH multimers. The Office admits that Potter *et al.* does not teach GnRH multimers with D-Lysine at residue 6. However, the GB Patent '262 and the GB patent '969 are alleged to disclose GnRH analogs in which residue 6 is a D-amino acid, such as D-Lysine. The Examiner has suggested that it would have been obvious to one of ordinary skill in the art to combine these references to generate the claims of the current invention.

Applicants wish to stress that Potter *et al.* only discloses recombinant leukotoxin GnRH fusion products (Examples 1-9; especially Examples 2-4). It is not possible to recombinantly produce a peptide of the current invention, because a peptide of the instant invention comprises at least one dextrorotatory amino acid. Dextrorotatory amino acids are not available in a biological expression system. As such, Potter *et al.* does not teach not suggest to use non-naturally occurring amino acids. A person of skill in the art, therefore, would not combine the recombinant leukotoxin-GnRH fusion products with the teachings of G.B. 2, 228,262 or G.B. 2,196,969. Claims 1 and 6-15, therefore, involve an inventive step.

The combination of Potter *et al.*, with the G.B. Patents, teaches and suggests the chimeric proteins of Potter *et al.* fused to a leukotoxin with amino acid 6 being a D-amino acid such as D-lysine. However, this does not teach all the elements of the instant claim 1. Claim 1 discloses two contiguous LHRH decapeptide sequences joined with a terminus to terminus linkage. Potter *et al.* teaches at least two contiguous LHRH sequences joined by a terminus to terminus linkage, (see claim 5) where this linkage is the C-terminal to N-terminal linkage between the LHRH decapeptides. Moreover, GB Patents '262 and '269, teach a dimer of the [D-amino acid^6]GnRH linked by the centrally located D-amino acid^6 side chains. The combination of the suggested prior art references Potter *et al.*, in light of the G.B. Patents '262 and '969, teach a at least two contiguous LHRH sequences joined by a centrally located D-amino acid^6 side chains. As such, the combination of references fails to teach or suggest all the elements of claim 1.

Applicants, therefore, submit that independent claim 1 is allowable over Potter *et al.* and the GB Patents '262 and '969, taken either individually or in combination, and respectfully requests reconsideration and allowance thereof.

Applicants further submit that claims 6-15 are allowable as being dependant from an allowable nonobvious independent claim1.

ENTRY OF AMENDMENTS

The proposed amendments to claims 1-5, 9, 10, 11, and 14 have been made according to the reissue amendment format governed by 37 CFR 1.173, and should be entered by the

examiner because, as described above, the amendments are supported by the as-filed specification and do not add any new matter to the application, Additionally, applicants assert that the amendments do not raise new issues or require further search. The amendments should place the reissue application in condition for allowance. To the extent they do not, however, they certainly remove issues for appeal and therefore should be entered.

CONCLUSION

In view of the proposed amendments and remarks, claims 1 through 15 are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Office determine that additional issues remain which might be resolved by a telephone conference, it is respectfully invited to contact applicants' undersigned agent.

Respectfully submitted,

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Enclosure: